were in the following order: PBS > SUPARTZ® > 1 injection of Gel-200 ≥ 2 injections of Gel-200. Efficacy of Gel-200 for suppression of cartilage degeneration was also demonstrated by a reduction of the increase in chondroitin 6-sulfate (6S) in the synovial fluid. In addition, Gel-200 appeared to improve the symptoms of synovitis, as judged from the reduction in increase of synovial fluid, protein and chondroitin 4-sulfate (4S) contents. Overall, since cartilage degeneration is milder when synovitis is not severe, these changes induced by Gel-200 may interact beneficially to relieve the progression of pathological changes. Histopathological findings of articular cartilage supported the morphological assessment. In the histopathological examination of synovium, cuboidal/stratified synovial epithelium, subepithelial cellular infiltration, subepithelial fibrosis/edema, subepithelial hemorrhage and subepithelial calcium deposition were observed in all the experimental groups. These changes were less severe in Gel-200 groups compared to those in the control group.
Conclusions: These data show that in a rabbit ACL transection model of OA, a single intra-articular injection of Gel-200 was superior to five injections of SUPARTZ® in slowing cartilage degeneration. It is considered that this superiority of Gel-200 is attributed to its highly cross-linked structure.

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THE IN VIVO ACTIVATION OF PPARγ BY THE LIGAND PIOGLITAZONE REDUCES THE DEVELOPMENT OF CARTILAGE LESIONS AND SYNTHESIS OF CATABOLIC FACTORS IN AN OSTEOARTHRITIS DOG MODEL

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Purpose: The peroxisome proliferator-activated receptor (PPAR)γ is a known modulator of a number of inflammatory pathways. Emerging evidence indicates that PPARγ may have protective effects on structural changes in osteoarthritis (OA). In this study we evaluated the in vivo therapeutic effect of a PPARγ agonist, pioglitazone, on the development of structural lesions in a dog anterior cruciate ligament (ACL) model of OA and explored the effect of the drug on the major synthetic pathways involved in the disease process.
Methods: OA was surgically induced in 24 dogs. The OA dogs were randomly divided into 3 groups (n=8 per group) and treated orally with either placebo, 15 mg/kg/day of pioglitazone, or 30 mg/kg/day of pioglitazone. The treatment began the day after surgery and continued for a period of 8 weeks. The severity of cartilage lesions was scored macroscopically. Cartilage specimens from femoral condyles and tibial plateaus were processed for histologic evaluation. Both cartilage and synovial membrane were processed for quantitative RT-PCR and immunohistochemistry. Specific probes and antibodies were used to study iNOS, MMP-1 and ADAMTS-5.
Results: Pioglitazone treatment reduced the development of cartilage lesions in a dose-dependent manner. There was a reduction in the lesion scores, and statistical significance was reached for the medial condyle; $p<0.04$ and 0.03 respectively for 15 and 30 mg/kg/day of pioglitazone. This decrease correlated with the cartilage histologic scores. Pioglitazone also significantly reduced the production of OA key mediators, iNOS, MMP-1 and ADAMTS-5 in cartilage.
Conclusions: This study demonstrated the efficacy of pioglitazone, a PPARγ agonist, at reducing articular lesions in a dog model of OA. These results provide a new possibility for therapeutic intervention in OA, in which in vivo activation of PPARγ inhibits major cartilage catabolic factors responsible for articular tissue degradation.

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AUTOLOGOUS OSTEOCHONDRAL GRAFTS IN THE TREATMENT OF FOCAL CHONDRAL DEFECTS OF THE FEMORAL HEAD. AN EXPERIMENTAL STUDY IN RABBITS

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Purpose: To investigate and compare the characteristics of the reconstructed articular surface microscopically and histologically after a time period of 6 weeks following the treatment of a focal defect of the right femoral head with subchondral drilling and autologous osteochondral transplantation in rabbits
Methods: A 2,5 mm diameter and 3 mm depth iatrogenic osteochondral defect in the anterolateral weight bearing area of the right femoral head was created in 12 rabbits. In a group of 6 rabbits the lesion was treated with autologous osteochondral transplantation. The donor site for the transplant was the lateral condyle of the ipsilateral knee joint. The other group of 6 rabbits was treated with subchondral drilling. Both groups were sacrificed after a time period of 6 weeks and specimens were evaluated histologically under the classification system of the ICRS. For statistical analysis we used the Mann - Wittney test
Results: According to the ICRS score statistical significance was found for all variables between the 2 groups (subchondral drilling 6 weeks vs autologous osteochondral transplantation 6 weeks): articular surface (p=0,049), matrix (p=0,003), cell distribution ($p<$ 0,0005), subchondral bone (p=0,010), cartilage mineralization (p=0,0) except cell population viability.
Conclusions: In cases of focal osteochondral defect of the femoral head in rabbits, reconstruction of the articular surface through autologous osteochondral graft transplantation gives superior macroscopical and histological results in comparison to subchondral drilling

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EFFECTS OF THE INTERLEUKIN-1 RECEPTOR ANTAGONIST ANAKINRA, ON PAIN AND GROSS PATHOLOGY IN THE MONOIODOACETATE MODEL OF OSTEOARTHRITIS

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Purpose: Interleukin-1 (IL-1) is thought to play a role in both the joint destruction seen in osteoarthritis (OA) and the pain that develops with the disease. The monoiodoacetate (MIA) model of osteoarthritis in the rat has been used as a model of OA pain and additionally, displays gross pathology and histologic changes that resemble some components of OA pathology. This study therefore uses the MIA model to examine the effect of the IL-1 receptor antagonist (IL-1RA) Anakinra on cartilage degradation and joint pain.
Methods: 20 male Lewis rats of 7 weeks of age were randomized into 2 experimental groups of n=10. The rats were then implanted with Alzet osmotic pumps (model 2ML) containing either vehicle (PBS) or IL-1RA at a dose of 90mg/kg per day. Three days after osmotic pump implantation the right knees of each rat were injected with 0.3mg of MIA in 50ul of saline and the left knees with 50ul of saline. 6 rats from each group were then measured for pain on days 1, 2, 3,8,10 and 14 post MIA injection by incapacitance testing. This measures the difference in paw weight bearing between the MIA and saline injected